

APPENDIX

IN THE CLAIMS:

1. (Amended Two Times) A method for *in vivo* delivery of a [desired composition] fusion protein into [a human or animal] the central nervous system (CNS) [or spinal cord], comprising administering to [the] a human or an animal a [composition] fusion protein having a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) [in association with at least a molecule having a biological function, wherein said molecule with a biological function comprises] recombinantly fused to a second protein, wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment C and at least the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C, and wherein said [composition is capable of] fusion protein undergoes *in vivo* retrograde axonal transport and transynaptic transport [into] in the CNS [or the spinal cord] of the human or animal [and of being delivered at different areas of the spinal cord].

2. (Amended) The method according to claim 1, wherein the [composition] fusion protein is administered into a muscle.

3. (Amended) The method according to claim 2, wherein the [composition] fusion protein is administered into a muscle in the vicinity of a neuromuscular junction.

5. (Amended) The method according to claim 1, wherein the [composition] fusion protein is administered into neuronal cells.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

8. (Amended) The method according to claim [6 or claim 7] 1, wherein the [molecule] second protein is selected from the group consisting of protein SMN, BDNF (Brain-derived neurotrophic factor), NT-3 (Neurotrophin-3), NT-4/5, GDNF (Glial cell-line-derived neurotrophic factor), IGF (Insulin-like growth factor), PNI (protease nexin I), SPI3 (Serine Protease Inhibitor protein), ICE (Interleukin-1 β converting enzyme), Bcl-2, GFP (green fluorescent protein), an endonuclease[s like I-SceI or CRE], an antibody [antibodies], or a drug[s] specifically directed against neurodegenerative diseases [such as latero spinal amyotrophy (LSA)].

9. (Amended) The method according to claim 8, wherein the composition comprises a combination of at least two of said [molecules] second proteins.

10. (Amended) The method according to claim 8, wherein the [molecule] second protein is located upstream from the fragment of tetanus toxin.

11. (Amended) The method according to claim 8, wherein the [molecule] second protein is located downstream from the fragment of tetanus toxin.

31. (Amended Two Times) A method for [the treatment of the] treating a central nervous system (CNS) [or spinal cord] disease comprising:

[preparing] administering to a patient in need thereof a composition comprising a fusion protein, wherein the fusion protein comprises a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein, wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment C and [a fraction of fragment B of] at least the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C, and wherein the fusion protein undergoes *in vivo* retrograde axonal transport and transynaptic transport when

administered to the patient [in a composition for the treatment of the CNS or spinal cord
disease; and

delivering the composition in a therapeutically effective manner].

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com